Amendments

Claims 2-11 have been amended to correct the objected-to informalities. Specifically, the term "The" has been substituted for the term "A" and in claim 7, the term "and" is inserted before "oncogen".

Claims 2, 4, 5 and 17 have been amended as follows. In claim 2, the term "predetermined" has been replaced with –selected--; in claim 4, "geometrical" has been replaced with –optical--; in claim 5, --optical—is inserted before "properties". Claim 17 is amended to recite that changes in the one or more optical properties reflected in the test data compared to the comparison data represent activity of the candidate optical contrast enhancing agent.

Claim Rejections

Rejection under 35 U.S.C. §112, second paragraph

Claims 2-11 and 17 stand rejected under 35 U.S.C. §112, second paragraph, for indefiniteness. It is believed that this rejection is obviated by the claim amendments.

Rejection under 35 U.S.C. §102(b)

Claims 17, 2, 4-5, 9 and 11 stand rejected under 35 U.S.C §102(b) as anticipated by Haglund et al. The Office Action states that Haglund teaches a method of identifying an optical contrast enhancing agent suitable for use in imaging of a tumor: an intact organism is exposed to the candidate optical enhancer, images of brain are taken before and after exposure to the optical enhancer and the "before" and "after" images are compared to assess changes in the brain with regard to optical changes over time. Applicants respectfully traverse this rejection.

Haglund does not teach a method of identifying an optical contrast enhancing agent. Rather, Haglund uses enhanced optical imaging with a known tumor contrast-enhancing agent, indocyanine green, to distinguish gliomas from adjacent normal tissue in human patients.

Haglund does not teach Applicant's claimed method which, in the last step, requires comparing test data acquired after exposing the biological tissue to a candidate optical enhancing agent to comparison data, whereby changes in the one or more optical

properties reflected in the test data compared with the comparison data represent activity of the candidate optical contrast enhancing agent. Applicant respectfully disagrees with the Examiner's reference to pages 309-310 as teaching *comparison of* "before" (dye exposure) and "after" (dye exposure) images (emphasis supplied). The reference describes a method for calculating a control percentage difference image and a post-dye injection percentage difference image that involves collecting control images before and after injection of the dye, selecting a single "control" image and subtracting this from the preinjection and postinjection images. Haglund teaches using optical imaging to identify areas with dye staining that are not visible to the human eye, but Haglund does not teach Applicant's method for identifying optical contrast enhancing agents.

Anticipation requires that each and every element of the claim be taught by the cited reference. In view of the above remarks, Applicant submits that Haglund does not anticipate his claimed invention. Accordingly, withdrawal of the 102(b) rejection is respectfully requested.

Rejections under 35 U.S.C §103(a)

Claims 17, 2-5, 7, 9 and 11 stand rejected for obviousness over Haglund et al in view of Hochman et al. Haglund teaches using optical imaging to identify areas with dye staining that are not visible to the human eye. Haglund does not teach or suggest Applicants' claimed method for identifying a contrast enhancing agent for reasons discussed above. Hochman et al teaches an optical imaging method for visualizing tumor tissue surrounding or adjacent to nerve tissue. Both Haglund and Hochman teach the use of a known dye, indocyanine green, for visualizing tumor tissue. On reading Haglund and Hochman together, one skilled in the art would be motivated to use indocyanine green for optical enhancement imaging of brain tumors, and would have a reasonable expectation of success in using nerve stimulation with this technique to locate and avoid damage to functional nerves during surgery. However, neither of the cited references alone or in combination teaches or suggests Applicant's claimed method for identifying a contrast enhancement agent, thus the method would not have been obvious to one skilled in the art at the time of the invention.

Accordingly, Applicant respectfully requests withdrawal of this ground of rejection of the claims under 35 U.S.C. §103.

Claims 17 and 3-11 stand rejected under 35 U.S.C. §103(a) as obvious over Verkman et al. The Office Action states that Verkman does not specifically teach a method of identifying an optical enhancer by comparing test data to comparison or control data. Nevertheless, it concludes that it would have been obvious to one of ordinary skill in the art to have compared the test data of cells loaded with a fluorescent marker (optical enhancer) to control data (of unloaded cells or cells loaded with different markers) to determine if a particular enhancer is cell impermeant and/or a better marker for ion transport, as taught and suggested by Verkman (pp. 105-106). Applicants respectfully traverse this rejection.

It is well established that the prior art must suggest the desirability of the claimed invention. Applicant believies that there is no teaching *or suggestion* in Verkman of Applicant's claimed method of identifying contrast enhancement agents. Verkman discloses that various membrane transport indicators have particular properties (e.g., he states that SPQ and fluorescein sulfonate were used as extracellular Cl-sensitive and insensitive indicators (p. 105), and that SPQ is membrane-impermeant (p.106)). These disclosures do not suggest anything about the method(s) by which the aforementioned properties were discovered. Consequently, the Examiner's conclusion of obviousness appears to be based upon an "obvious-to-try" standard. This is not a proper legal standard for judging obviousness.

Accordingly, the Applicant respectfully requests that the Examiner withdraw this ground of rejection of the claims under 35 U.S.C. §103(a).

Conclusion

The Examiner's objections and rejections of the claims have been addressed, and it is believed that all of the pending claims are in condition for allowance. Early reconsideration and allowance of the pending claims is respectfully requested.

Respectfully submitted,

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